REMARKS

In view of the present Official Action, Claims 1, 2, 4, 5, 7, 9, 11, 13, 17, 18, 21, 23 and 25 are pending; Claims 22, 24 and 26 have been cancelled; and Claims 1, 9 and 13 have been amended to recite a second probiotic organism being different than the first probiotic organism. Support for these amendments can be found throughout the specification, such as page 8 line 20 to page 9 line 22. No new matter has been entered into the disclosure by way of the above amendments.

Claims 1, 2, 4, 5, 7, 9, 11, 13, 21, 23 and 25 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over U.S. Patent 6,468,526 to Chrisope et al. (hereinafter, "Chrisope") as evidenced by *Probiotics and prebiotics: Can regulating the activities of intestinal bacteria benefit health?* BMJ 1999: 318:999-1003 by MacFarlane et al. (hereinafter, "MacFarlane") in view of U.S. Patent 7,220,18 to Hans et al. (hereinafter, "Hans") and further in view of *Journal of Systematic Bacteriology*, 217-221, 1999 by Falsen et al. (hereinafter, "Falsen").

Claims 17 and 18 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Chrisope in view of Hans and Falsen as applied to Claims 1, 2, 4, 5, 7, 9-11 and 13 and further in view of MacFarlane.

Claims 21- 26 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement.

In view of the following remarks, Applicants request further examination and reconsideration of the present patent application.

Rejections under 35 U.S.C. §112

Claims 21- 26 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. In response, Applicants respectfully submit that

Lactobacillus iners Y16329 is fully understood by one of ordinary skill in the art. The nucleotide sequence for *Lactobacillus iners* Y16329 can be found through the publicly available GenBank database. A copy of the output provided by the GenBank database for *Lactobacillus iners* Y16329 is attached. The knowledge of one of ordinary skill in the art is further evidenced by the Falsen article, as noted on page 3 of the Official Action. Claims 22, 24 and 26 have been cancelled, without prejudice.

Withdrawal of the rejection and allowance of Claims 21, 23 and 25 are earnestly solicited.

Rejections Under 35 U.S.C. §103

Claims 1, 2, 4, 5, 7, 9, 11 and 13 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Chrisope as evidenced by MacFarlane in view of Hans and further in view of Falsen.

This combination of references does not render the claimed invention *prima facie* obvious.

Chrisope discloses a bacterium of the genus Lactobacillus with purportedly desirable characteristics suitable for use in a vaginal medicament. See column 2 lines 50-52 of Chrisope. Chrisope further discloses that the *crispatus* and *jensenii* strains of *Lactobacillus* are superior to other strains for use in a vaginal medicament. See column 7 lines 39-42 of Chrisope. Chrisope also discloses application of a clindamycin cream followed by repeated applications of a single type of Lactobacillus suppository containing the same *Lactobacillus crispatus* CTV-05 strain to treat women with recurrent bacterial vaginosis (BV). See column 31 lines 28 to 33 of Chrisope. Chrisope does not teach or suggest the use of *Lactobacillus iners*.

Moreover, Chrisope does not teach or suggest administration of a therapeutically effective amount of a second probiotic organism, the second probiotic organism being different than the first probiotic organism, as recited in Claims 1, 9, 13 and all claims depending therefrom of the present application. In contrast, Chrisope merely discloses a first administration of *L. crispatus* CTV-05 capsule followed by repeated doses of the same *L. crispatus* CTV-05 capsule.

The Official Action contends that Falsen discloses *Lactobacillus iners*. Falsen apparently discloses identification of several strains of *Lactobacillus* isolated from human sources. See lines 1-5 right hand column page 218 of Falsen. Falsen states that Lactobacilli are important commercially, based on the growing interest in their use as probiotics, but Falsen does not teach or suggest a method or treatment involving *Lactobacillus* or the specific strain *iners*. See lines 8-12 left hand column page 217 of Falsen. More specifically, Falsen does not teach or suggest treatment or methods of establishing healthy bacterial flora through a treatment of a first probiotic, *Lactobacillus iners,* and a second probiotic, as recited in Claims 1, 9, 13 and all claims depending therefrom of the present application. Further, Falsen does not teach or suggest administration of a therapeutically effective amount of a second probiotic organism, the second probiotic organism being different than the first probiotic organism, as recited in Claims 1, 9, 13 and all claims depending therefrom of the present application.

MacFarlane discloses commercial preparations of lactobacilli. See right column page 999 of MacFarlane. MacFarlane does not teach or suggest specific strains of Lactobacilli, including *iners*, further, MacFarlane does not teach or suggest treatment or methods of establishing healthy bacterial flora through a treatment of a first probiotic, *Lactobacillus iners*, and a second probiotic, as recited in Claims 1, 9, 13 and all claims depending therefrom of the present application. Further still, MacFarlane does not teach or suggest administration of a

therapeutically effective amount of a second probiotic organism, the second probiotic organism being different than the first probiotic organism, as recited in Claims 1, 9, 13 and all claims depending therefrom of the present application.

Hans discloses the secretion *in vivo* of trefoil peptides by microorganisms for treatment of inflammatory disorders of the gastro-intestinal tract, including the use of Lactobacillus *iners* as the microorganism to deliver the peptide. See column 1 lines 12-19 and column 2 line 49 to column 3 line 52 of Hans. Hans does not teach or suggest treatment or methods of establishing healthy bacterial flora through a treatment of a first probiotic, *Lactobacillus iners*, and a second probiotic, as recited in Claims 1, 9, 13 and all claims depending therefrom of the present application. Further, Hans does not teach or suggest administration of a therapeutically effective amount of a second probiotic organism, the second probiotic organism being different than the first probiotic organism, as recited in Claims 1, 9, 13 and all claims depending therefrom of the present application.

Further, page 5 of the Official Action alleges that administration of *L. crispatus* CTV-05 would be reasonably expected to treat or prevent vaginal infections for the same reason as *Lactobacillus iners* because they are both non-pathogenic strains of the genus Lactobacillus. Microorganisms are extremely complex and do not necessarily act in a predictable way. Comparing the above statement to the pharmaceutical field, a comparatively small change in structure, or a small change to a substituent group can cause very large changes in effect. The Official Action has not provided any reason or evidence that *L. crispatus* CTV-05 would be reasonably expected to treat or prevent vaginal infections for the same reason as *Lactobacillus iners*.

It would not have been obvious to one of ordinary skill in the art to substitute the *Lactobacillus* strain *iners* as described in Falsen with the strains described in Chrisope. This substitution would not have been obvious, because not only did the inventors of Chrisope not know of or consider the effects and use of this other strain in their disclosure, the *iners* strain was discovered 1 year after the original filing in the Chrisope case. Further, the strain *iners* is phylogenetically quite distinct, and has several different reactions to mediums of growth as taught by Falsen.

Since none of the Chrisope, MacFarlane, Hans and Falsen references singularly teach or suggest administration of a therapeutically effective amount of a second probiotic organism, the second probiotic organism being different than the first probiotic organism, as recited in Claims 1, 9, 13 and all claims depending therefrom of the present application, the combination of references will not teach this claim recitation. Thus, the rejection of Claims 1, 2, 4, 5, 7, 9, 11 and 13 under 35 U.S.C. §103(a) is overcome. Withdrawal of the rejection and issuance of Claims 1, 2, 4, 5, 7, 9, 11 and 13 is earnestly solicited.

Claims 17 and 18 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Chrisope in view of Hans and Falsen as applied to Claims 1, 2, 4, 5, 7, 9-11 and 13 and further in view of MacFarlane.

Claims 17 and 18, which depend on Claim 7, are not rendered obvious by the combination of Chrisope, Hans, Falsen and MacFarlane because the combination of references do not teach or suggest treatment or methods of establishing healthy bacterial flora through a treatment of a first probiotic, *Lactobacillus iners*, and a second probiotic, as recited in Claims 1, 7 and all claims depending therefrom of the present application. Further, the above combination of references do not teach or suggest administration of a therapeutically effective amount of a

second probiotic organism, the second probiotic organism being different than the first probiotic organism, as recited in Claim 1 and all claims depending therefrom of the present application. Further still, the combination of references do not teach or suggest a prebiotic being inulin or fructo-oligosaccharides or milk.

Further, a prebiotic is a non-metabolized, non-absorbed substrate that is useful for the host which selectively enhances the growth and/or the metabolic activity of a bacterium or a group of bacteria. A prebiotic also includes a nutrient utilized by lactobacilli or bifidobacteria to stimulate and/or enhance growth of lactobacilli or bifidobacteria relative to pathogenic bacteria. See page 8 lines 7-11 of the present application. Clindamycin is an antibiotic. Antibiotics kill or inhibit the growth of microorganisms. Clindamycin does not include a nutrient utilized by lactobacilli. Thus, the treatment as purportedly disclosed by Chrisope, which requires a first administration of clindamycin, does not teach or suggest a prebiotic as recited in Claim 7, from which Claims 17 and 18 depend, of the present application.

Since none of the Chrisope, MacFarlane, Hans and Falsen references singularly teach or suggest administration of a therapeutically effective amount of a second probiotic organism, the second probiotic organism being different than the first probiotic organism, as recited in Claim 1 and all claims depending therefrom of the present application, the combination of references cannot teach or suggest this claim recitation. Thus, the rejection of Claims 17 and 18 under 35 U.S.C. §103(a) is overcome. Withdrawal of the rejection and issuance of Claims 17 and 18 is earnestly solicited.

Since none of the references singularly teach or suggest administration of a therapeutically effective amount of a second probiotic organism, the second probiotic organism being different than the first probiotic organism, as recited in Claims 1, 9, 13 and all claims

depending therefrom of the present application, the combination of references do not remotely recognize this claim recitation.

It is respectfully submitted that the foregoing amendments and remarks effectively address each of the issues underlying the Examiner's rejections. Withdrawal of all outstanding objections and rejections is respectfully requested. It is therefore respectfully suggested that the claims are in condition for allowance, and that allowance is respectfully requested.

Respectfully submitted,

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